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Dr. Aaron Shatkin
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Dear Aaron:

I am responding to your request for something in writing about biohazards of recombinant DNA molecules.

On philosophical grounds I believe in free scientific inquiry, as I believe in freedom of speech, limited only by a "clear and present danger" of harm. This belief is rooted in the conviction that free inquiry harmonizes best with the human spirit, and that in the long run it benefits people maximally. (I don't think it is special pleading to say that the type of inquiry we are concerned with is likely to be of considerable long range benefit.) The implications for our immediate problem are 1) that we should encourage research involving DNA recombinants, since this appears to be of high promise; 2) that no line of inquiry should be prohibited unless there is a clear and present danger of harmful effect; and 3) that we must foresee as best we can the harm that may come from different types of experiments with recombinant DNA, and devise conditions under which such experiments can proceed.

In regard to the first two points, it obviously goes counter to arguments (heard at our recent meeting and elsewhere) that certain experiments involving recombinant DNA molecules should not be done because on scientific grounds there is no need to do them or they have low potential benefit. The right to decide this type of question is the heart of free inquiry and must be left to the individual scientist; correctness of his intuition and experimental tactics will be judged in due course. Another implication of free inquiry is that the current moratorium should end, leaving not a free for all, but a set of guidelines based on assessment of possible harm.

Obviously, assessment of risk is, and will likely always be, based on inadequate data, and this is the crux of our problem. However, it is not much different from similar problems we have lived with for some time, e.g., the potential hazards of microbes and their mutants, particularly mutants of pathogenic microbes. Earlier fears of the creation of highly virulent pathogens by genetic manipulation

have not been realized, even though "human" viruses like poliovirus, influenza, reovirus, and adenoviruses, and different enteric bacilli have been extensively manipulated, often in the open laboratory. Clearly, DNA manipulation extends the possibilities much further.

How then does one classify experiments according to risk? In my opinion, a good place to start is with the National Cancer Institute's classification of oncogenic viruses, generalized to types of experiments with recombinant DNA molecules. We should try to define minimal, moderate, and high risk classes of experiments and then develop guidelines indicating the conditions under which each class of experiment should be carried out. I hope the classes can be sufficiently general so that a given biohazard classification can include viruses, bacteria, and other microbes, as well as recombinant DNA, with a single set of procedural requirements for all "agents" in that category. I believe that most experiments with recombinant DNA's are likely to be classified as nonhazardous or minimally hazardous, some as moderately hazardous, and at present, very few as highly hazardous. Clearly, proposed definitions of these categories and the procedural requirements for each need to be hammered out by a working group of scientists, hopefully at the Conference. Although I have some thoughts on this, it is hard to be rigid when nearly everything is based on judgments of risk and judgments of the effectiveness of procedures for decreasing the risk. However, there is some relevant data with infectious agents and here is one area where experiments can be done to provide more information, e.g., on infectivity of DNA in animals, spread of plasmids from different E. coli mutants or persistence of a bacterial or viral carrier, etc.

How to enforce the guidelines? In spite of drawbacks, I see no feasible alternative to local institutional biohazard committees which monitor all biohazardous research and certify in writing that each such program conforms to the general guidelines. All granting agencies and the institution itself should require such certification, thus leaving legal responsibility and consequent pressure to conform with the institution.

In closing let me tell you what I hope will emerge from the Asilomar Conference. First, a positive statement about the potential benefits of using recombinant DNA and the importance of encouraging research using this methodology. Second, a sober statement on potential hazards, emphasizing the hypothetical nature of these hazards and citing relevant experience with microbes and their mutants.

Third, a set of guidelines, defining classes of experiments ranging from "no risk" to "high risk" and procedures to be followed in each category. Fourth, a recommendation to all research granting agencies and institutions that these guidelines be adopted and that they be monitored (and compliance certified) by institutional biohazard committees.

With best regards,

Sincerely,

Daniel Nathans

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